IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-1282)

In the Application of:	
Jourdier et al.	**Examiner: Bao Q. Li**
Serial No.: 09/720,513	**Group Art Unit: 1648**
Filing Date: March 26, 2001	**Confirmation No.: 1648**
For: Mucosal Targeting Immunisation	

DECLARATION OF THERESE-MARIE JOURDIER UNDER 37 C.F.R. § 1.132

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Therese-Marie Jourdier, declare as follows:

1. I am a named inventor of the above-captioned patent application.

2. I have a doctorate in Microbiology, specializing in virology. My doctoral thesis was entitled, "Establishment of experimental animal models for the study of the infection by the virus Herpes simplex."

3. I am currently in the Research / Immunology Department of Aventis Pasteur S.A. I have been employed by Aventis Pasteur S.A. and its predecessor companies since 1975, when I began working in the microbiology department. Since 1983 my work has centered on the establishment of animal models to access inoculation parameters and immunogenicity of antigens under consideration by our company.

4. Based on my education and 20 years of experience referred to above, I am considered an expert in animal experimentation, being authorized by the French Agriculture and Fishing Ministry (sub-direction of Health and Animal Protection) to undertake and supervise experimentation on a large panel of live vertebrate animals.

5. On information and belief I understand that the U.S. patent examiner has alleged that the data on page 19 and 20 of the specification (which show that an intramuscular

injection in the thigh induces a much greater immune response in the rectogenitourinary lymph node system and mucous membranes compared to the submaxillary and axillary lymph nodes and in the blood (page 19) and induces a specific IgG and IgA immune response (page 20)) is not unexpected because one would expect a greater immune response nearer the area of administration. On information and belief I also understand that the examiner has asserted that the experiments on page 19 and 20 do not have a control.

6. To address the examiner's concerns, I present herein the results of an experiment in which the HIV-1 gp160 MN/LAI antigen was administered with an adjuvant to four monkeys.

Group 1: administration was by vaginal and rectal routes simultaneously with 100 µg of adjuvanted antigen according to the administration regimen 1 (Appendix 1).

Groups 2 and 3: administration was by intramuscular injection in the rectus femoris of ALVAC vCP205 10^6CCID50 per thigh and 50 µg of adjuvanted antigen/thigh (group 2) followed by vaginal and rectal routes simultaneously with 100 µg of adjuvanted antigen (group 3) according to the administration regimen 2 (Appendix 2).

Groups 4 and 5: administration was by intramuscular injection in the gracilis of ALVAC vCP205 10^6CCID50 per thigh and 50 µg of adjuvanted antigen/thigh (group 4) followed by vaginal and rectal routes simultaneously with 100 µg of adjuvanted antigen (group 5) according to the administration regimen 2.

7. Samplings of vaginal and rectal secretions were taken regularly for quantitation of local antibodies at the same time that blood samplings were taken for quantitation of serum antibodies. Seven days after the last immunization, the animals were euthanized for quantitation of specific antibody producing cells in various lymph nodes. The analysis of the immune response was carried out by the same methods as described in the present specification. The results obtained are given in table 1 (appendix 3) and represent (per group) the average of the results obtained from the four monkeys.

8. The results obtained show that:

(a) No specific IgG and IgA were present in the vaginal or rectal secretions when the antigens were administered directly at the targeted site where the immune response is expected.

(b) Specific IgA and IgG were induced when the antigens were administered by intramuscular injection in the thigh; vaginal and rectal additional injection did not boost the initial immune response.

9. .One would expect to improve the immune response at the targeted mucosal site by administering the antigen directly at said site but the data provided here shows that the immune response is improved only when the administration site allows the priming of the draining lymph nodes this means when the antigen is administered intramuscularly in the thigh.

10. To my knowledge, there is no basis by which one of ordinary skill in the art could have expected that administration to the thigh would result in a specific targeted response in an area distal from the site of administration in general and in the rectogenitourinary lymph node system and mucous membranes in particular. The data presented herein support this point as they demonstrate that one cannot even expect a specific immune response at the site of administration.

11. I further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Sec. 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

T M Jourdier

Therese-Marie Jourdier

Date: Feb 8, 2005